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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,600	10/28/2003	Dennis A. Steindler	7203-8	6329

7590 03/14/2007
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EXAMINER

SAJJADI, FEREDOUN GHOTB

ART UNIT	PAPER NUMBER
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1633

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 1, 2007 that includes a response to the final office action dated November 1, 2006, has been entered: Claims 30-32 and 35-37 have been amended, and claims 33-34 and 38-39 have been cancelled. No new claims were added.

Claims 30-32, and 35-37 remain pending in the application and are under current examination.

Non Compliance with 37 CFR 1.121

The amendment filed on February 1, 2006 is objected to under 37 CFR 1.121(c). Claim 1, contains the newly added claim text: "wherein the brain stem cells are from a mammal selected from the group consisting of human and mouse", without underlining marking the changes, and is therefore not in compliance with 37 CFR 1.121(c). While the amendment has been entered, please note that compliance with 37 CFR 1.121 is required for all future claim amendments. Failure to comply may result in non-entry of the amendment.

Response to Claim Rejections - 35 USC § 112- Second Paragraph

Claims 30-39 were previously rejected in the office action dated November 1, 2006, under 35 USC § 112- Second Paragraph, as being indefinite. Applicants' cancellation of claims 33-34 and 38-39 renders their rejection moot. Applicants' amendment of base claim 30, deleting language referring to the appearance of the stem cells, obviates the grounds of rejection; and further in view of Applicants' cancellation of claims 38-39, the rejection of claim 30-32 and 35-37 is hereby withdrawn.

Response to Claim Rejections - 35 USC § 112, Written Description

Claims 30-39 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Applicants' cancellation of claims 33-34 and 38-39 renders their rejection moot. The rejection set forth on pp. 3-4 of the previous office action dated November 1, 2006 is maintained in part, for claims 30-32, and 35-37, for reasons of record.

Applicants argue that as amended claim 30 recites "an *ex vivo* culture of an isolated population of multipotent, progenitor or precursor brain stem cells that are immunonegative for glial fibrillary protein, nestin and TuJ1 when cultured under conditions that prevent or reduce cell-cell and cell-substrate interactions; wherein the brain stem cells are from a mammal selected from the group consisting of human and mouse", and because the language of the dependent claims has also been amended to recite mouse instead of murine, withdrawal of the rejection is requested. Applicants' arguments have been fully considered, but are not found persuasive.

While the current amendments partially overcome the grounds for rejection, the claims continue to read on isolated multipotent brain stem cells that are immunonegative for GFP, nestin and TuJ1. As set forth in the previous office action, the instant specification only demonstrates possession of a mixed population of human or mouse brain progenitor cells, and further, Applicants have failed to demonstrate possession of any isolated cell types, given that the mixed culture of brain multipotent progenitor cells represent a continuum of cell proliferation and differentiation, wherein different cell types are simultaneously immunonegative for said markers. As such, no population of cells may be demonstrated as isolated.

Hence, the rejection of claims 30-32, and 35-37 is maintained for reasons of record and the foregoing discussion.

Response to Claim Rejections - 35 USC § 112-Lack of Enablement

Claims 30-39 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. Applicants' cancellation of claims 33-34 and 38-39 renders their rejection moot. The rejection set forth on pp. 4-5 of the previous office action dated November 1, 2006 is maintained for claims 30-32, and 35-37, for reasons of record.

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Applicants disagree with the rejection and having cited MPEP 2168.08 and 2154.01 regarding the test of enablement, assert that because of the high level of skill in the art and the state of the art at the time the application was filed, one of ordinary skill in the art would not have to perform undue experimentation to make and use the invention as claimed. Applicants further argue that the amended claims overcome the rejections, because the specification does describe the isolation and culturing of an isolated population of multipotent, progenitor or precursor brain stem cells that are immunonegative for glial fibrillary protein, nestin and TuJ1 when cultured under conditions that prevent or reduce cell-cell and cell-substrate interactions, wherein the brain stem cells are from a mammal selected from the group consisting of human and mouse. Applicants' arguments have been fully considered, but are not found persuasive.

In response, it is noted that the instant application claims priority to January 7, 1997. As such, the isolation of brain stem cells by a person of ordinary skill in the art at the time of filing was neither routine, nor predictable, as previously indicated by Gage et al. (of record). Further, as set forth in the previous office action, the instant application's disclosure does not provide an enablement for the isolation of multipotent brain stem cells.

Applicants' specification states: "The different types of clones observed in the cultures described above and in the experiments described below, represent a continuum of cell proliferation and differentiation, with the existence of both early and late type II clones...that eventually differentiate into type III clusters...The potential for numerous, undefined hematopoietic stem cells still exists...The use of just one feature as an identification tool can occur, although it makes the recognition of the specific stem cell type rather tenuous" (lines 7-17, p. 12). Therefore, the instantly claimed *ex vivo* culture of cells contains type III cells that are not immunonegative for GFP, nestin and TuJ1.

The instant specification describes the mixed culture of a population of cellular aggregates described as type I, type II and type III (p. 7, lines 16 and 17). The specification describes the dissociation of brain tissue and subsequent propagation of the cells in suspension cultures and concludes: "some type II cells are also present in these cultures" (Example 1, last paragraph). The specification does not describe either the isolation or the purification of a population of cells that are immunonegative for the markers tested (or may be described as type I, in the absence of other cell types). Moreover, it is apparent from the preceding that the culture

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of brain stem cells contains both type I and type II clones. Type II clones do not attach to either plastic or laminin-coated substrates and become positive for the nestin (p. 8). A definitive test to show isolation of a population of immunonegative type I clones, would require their purification from the mixed culture, and subsequent differentiation into type II and type III clones.

Applicants claim a product that is only defined in structure by negative limitations. In the absence of any known positively displayed cell surface markers, the purification of type I clones would require additional experimentation, without any guarantee of success.

In conclusion, a mixed population of cell aggregates may not be correctly described as "isolated multipotent stem cells", even when the term population is included in the description. Hence, the rejection of claims 30-32 and 35-37 is maintained for reasons of record and the foregoing discussion.

Examiner's Comment

Applicants should note that if the instant claims are amended to recite "a mixed population of *ex vivo* cultured multipotent brain stem cells", the claims may become subject to rejection over the prior art made of record and not relied upon.

Conclusion

Claims 30-32 and 35-37 are not allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period

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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst William Phillips, whose telephone number is **(571) 272-0548**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at **(800) 786-9199**.

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PRIMARY EXAMINER

